RENAMIN - leucine, phenylalanine, lysine, methionine, isoleucine, valine, histidine, threonine, tryptophan, alanine, glycine, arginine, proline, tyrosine and serine injection

Baxter Healthcare Corporation

DESCRIPTION

RenAmin® (Amino Acid) Injection is a sterile, nonpyrogenic, hypertonic solution of essential and nonessential amino acids in a Pharmacy Bulk Package. A Pharmacy Bulk Package is a container of a sterile preparation for parenteral use that contains many single doses. The contents are intended for use in a pharmacy admixture program and are restricted to the preparation of admixtures for intravenous infusion.

Each 100 mL of RenAmin® (Amino Acid) Injection contains:

Amino Acids	6.5 g
Total Nitrogen	1 g
pH (pH adjusted with glacial acetic acid)	6.0 (5.0 to 7.0)

Essential Amino Acids

Valine - $C_5H_{11}NO_2$	820 mg
Leucine - $C_6H_{13}NO_2$	600 mg
Isoleucine - $C_6H_{13}NO_2$	500 mg
Methionine - $C_5H_{11}NO_2S$	500 mg
Phenylalanine - $C_9H_{11}NO_2$	490 mg
Lysine (added as the hydrochloride salt) - $C_6H_{14}N_2O_2$	450 mg
Histidine - $C_6H_9N_3O_2$	420 mg
Threonine - $C_4H_9NO_3$	380 mg
Tryptophan - $C_{11}H_{12}N_2O_2$	160 mg

Nonessential Amino Acids

Arginine – $C_6H_{14}N_4O_2$	630 mg
Alanine – $C_3H_7NO_2$	560 mg
Proline – $C_5H_9NO_2$	350 mg
Glycine – $C_2H_5NO_2$	300 mg
Serine – $C_3H_7NO_3$	300 mg
Tyrosine-$C_9H_{11}NO_3$	40 mg

Anion Profile per Liter*

Acetate (1)	60 mEq
Chloride (2)	31 mEq

* Balanced by ions from amino acids
(1) derived from pH adjustment with glacial acetic acid
(2) contributed by the Lysine Hydrochloride

3 mEq/L sodium bisulfite added as stabilizer

Osmolarity (calc.) 600 mOsmol/L

CLINICAL PHARMACOLOGY

RenAmin® (Amino Acid) Injection provides biologically utilizable source material for protein synthesis when used with appropriate calorie sources (such as hypertonic dextrose or fat emulsion), electrolytes, vitamins and minerals.

As a concentrated source of essential amino acids, RenAmin® (Amino Acid) Injection provides maximal protein intake with low volume administration. The essential amino acids are included as approximately 60% w/w of total amino acids. Each 250 mL unit of this injection meets or exceeds the recommended daily intake of essential amino acids. Nonessential amino acids have been included to meet requirements established in investigations of acute and chronic renal failure patients fed parenterally. The 40% w/w of nonessential amino acids includes histidine (considered an essential amino acid in renal failure), arginine, and other nonessential amino acids as additional sources of nitrogen that have been shown to enhance nitrogen balance and weight gain.

INDICATIONS AND USAGE

RenAmin® (Amino Acid) Injection is indicated as an adjunct in the offsetting of nitrogen loss or in the treatment of negative nitrogen balance in potentially reversible renal decompensation when the alimentary tract cannot or should not be used; gastrointestinal absorption of protein is impaired; or metabolic requirements for protein are substantially increased, as with extensive burns.

CONTRAINDICATIONS

Severe uncorrected electrolyte and acid base imbalance
Severe liver disease or hepatic coma
Hyperammonemia
Hypersensitivity to one or more amino acids
Decreased circulating blood volume

WARNINGS

This injection is for compounding only, not for direct infusion.

Proper administration of RenAmin® (Amino Acid) Injection requires a knowledge of fluid and electrolyte balance and nutrition as well as clinical expertise in recognition and treatment of the complications which may occur.
Administration of amino acid solutions to a patient with hepatic insufficiency may result in serum amino acid imbalances, hyperammonemia, stupor and coma.
Hyperammonemia is of **special significance in infants.** This reaction appears to be related to a deficiency of the urea cycle amino acids of genetic or product origin. It is essential that blood ammonia be measured frequently in infants.
This injection has no added electrolytes. Clinically significant hypocalcemia, hypophosphatemia or hypomagnesemia may occur. Electrolyte replacement may become necessary.
Contains sodium bisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.
This injection should not be administered simultaneously with blood through the same infusion set because of the possibility of pseudoagglutination.

RenAmin® (Amino Acid) Injection does not replace dialysis and conventional supportive therapy in patients with renal failure.
WARNING: This product contains aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.
Research indicatesthat patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 μg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

PRECAUTIONS

It is essential to provide adequate calories concurrently if parenterally administered amino acids are to be retained by the body and utilized for protein synthesis. Concentrated dextrose solutions are an effective source of such calories.

With the administration of RenAmin® (Amino Acid) Injection in combination with highly concentrated dextrose solutions, hyperglycemia, glycosuria and hyperosmolar syndrome may result. Blood and urine glucose should be monitored on a routine basis in patients receiving this therapy.
Sudden cessation in administration of a concentrated dextrose solution may result in insulin reaction due to continued endogenous insulin production. Parenteral nutrition mixtures should be withdrawn slowly.

Electrolytes may be added to RenAmin® (Amino Acid) Injection as dictated by the patient's electrolyte profile.
Strongly hypertonic nutrient solutions should be administered through an indwelling intravenous catheter with the tip located in the superior vena cava.
Care should be taken to avoid excess fluid accumulation, particularly in patients with renal disease, pulmonary insufficiency and heart disease.
During amino acid administration in the absence of supporting carbohydrate metabolism, an accumulation of ketone bodies in the blood often occurs. Correction of ketonemia usually can be accomplished by administering some carbohydrates.
Drug product contains no more than 25 μg/L of aluminum.

Laboratory Tests

Frequent clinical evaluation and laboratory determinations are necessary for proper monitoring during administration.
Studies should include blood urea nitrogen, blood sugar, serum proteins, kidney and liver function tests, electrolytes, acid-base balance, hemogram, carbon dioxide combining power or content, serum osmolarities, blood cultures and blood ammonia levels. Circulating blood volume should be determined, if indicated.

Carcinogenesis, Mutagenesis, Impairment of Fertility:

Studies with RenAmin® (Amino Acid) Injection have not been performed to evaluate carcinogenesis potential, mutagenic potential, or effects on fertility.

Pregnancy:

Teratogenic Effects

Pregnancy Category C.

Animal reproduction studies have not been conducted with RenAmin® (Amino Acid) Injection. It is also not known whether RenAmin® (Amino Acid) Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. RenAmin® (Amino Acid) Injection should be given to a pregnant woman only if clearly needed.

Nursing Mothers:

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for adverse reactions, e.g., hyperammonemia in nursing infants, caution should be exercised when RenAmin® (Amino Acid) Injection is administered to a nursing mother.

Pediatric Use:

Safety and effectiveness of RenAmin® (Amino Acid) Injection have not been established by adequate and well-controlled studies in pediatric patients.

Geriatric Use:

Clinical studies of RenAmin® (Amino Acid) Injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from other younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

SPECIAL PRECAUTIONS

Administration of amino acid solutions and other nutrients via central or peripheral venous catheter may be associated with complications which can be prevented or minimized by careful attention to all aspects of the procedure. This includes attention to solution preparation, administration and patient monitoring. **It is essential that a carefully prepared protocol, based on current medical practices, be followed, preferably by an experienced team.**

Although a detailed discussion of the complications is beyond the scope of this insert, the following summary lists those based on current literature:

Technical:

The placement of a central venous catheter should be regarded as a surgical procedure. The physician should be fully acquainted with various techniques of catheter insertion as well as recognition and treatment of complications. For details of techniques and placement sites consult the medical literature. X-ray is the best means of verifying catheter placement. Complications known to occur from the placement of central venous catheters are pneumothorax, hemothorax, hydrothorax, artery puncture and transection, injury to the brachial plexus, malposition of the catheter, formulation of arteriovenous fistula, phlebitis, thrombosis, cardiac arrhythmia and catheter embolus.

Septic:

The constant risk of sepsis is present during administration of parenteral nutrition solution. Since contaminated solutions and infusion catheters are potential sources of infection, it is imperative that the preparation of the solution and the placement and care of catheters be accomplished under controlled aseptic conditions. If fever develops, the solution, its delivery system and the site of the indwelling catheter should be changed.

Metabolic:

The following metabolic complications have been reported: metabolic acidosis, hypophosphatemia, alkalosis, hyperglycemia and glycosuria, osmotic diuresis and dehydration, rebound hypoglycemia, elevated liver enzymes, hypo- and hypervitaminosis, electrolyte imbalances and hyperammonemia. Frequent clinical evaluation and laboratory determinations are necessary, especially during the first few days of therapy, to prevent or minimize these complications.

Special Precautions in Patients with Renal Insufficiency
Frequent laboratory studies are necessary in patients with renal insufficiency. In renal failure, hyperglycemia may not be reflected by glycosuria. Blood glucose must be determined frequently, often every six hours to guide dosage of dextrose, and insulin should be given, if required.

Special Precautions in Pediatric Patients

RenAmin® (Amino Acid) Injection should be used with special caution in pediatric patients with acute renal failure, especially low birth weight infants. Laboratory and clinical monitoring of pediatric patients, especially those who are nutritionally depleted, must be extensive and frequent. See Children section under DOSAGE AND ADMINISTRATION for additional information. Frequent monitoring of blood glucose is required in low birth weight or septic infants, as hypertonic dextrose infusion involves a greater risk of hyperglycemia in such patients.

ADVERSE REACTIONS
See WARNINGS and PRECAUTIONS
Adverse effects include metabolic, electrolyte, acid-base and fluid imbalances unless special care with monitoring and corrective management is maintained during RenAmin® (Amino Acid) injection administration.
Infusion of any hypertonic solution can result in local inflammatory reactions. Policies and procedures should be established for the recognition and management of such reactions.

DOSAGE AND ADMINISTRATION
If a patient is unable to take oral nourishment for a prolonged period of time, institution of total parenteral nutrition (TPN) with exogenous calories should be considered.
Fat emulsion coadministration should be considered when prolonged (more than 5 days) parenteral nutrition is required in order to prevent essential fatty acid deficiency (EFAD). Serum lipids should be monitored for evidence of EFAD in patients maintained on fat free TPN.

Adult:

The total daily dose of RenAmin® (Amino Acid) Injection depends on the patient's metabolic requirement and clinical response. The determination of nitrogen balance and accurate daily body weights, corrected for fluid balance, are probably the best means of assessing individual nitrogen requirements.
Nutritional management of renal decompensation includes providing sufficient amino acid and caloric support for protein synthesis while not exceeding renal capacity for excretion of metabolic wastes. A dosage of 2.5 to 5.0 grams of nitrogen per day with adequate calories will maintain nitrogen equilibrium in most patients with uremia. If more nitrogen and calories are required, higher dosages may be administered, provided great care is taken to avoid exceeding limits of fluid intake or glucose tolerance.
Dosage should be guided by fluid, glucose and nitrogen tolerances, as well as metabolic and clinical responses. The rate of increase in blood urea nitrogen concentration generally diminishes when infusion of amino acids is accompanied by adequate calories. However, excessive intake of protein or increased protein catabolism may alter this response.

The usual daily dose ranges from 250 to 500 mL of RenAmin® (Amino Acid) Injection equivalent to 2.5 to 5.0 grams of nitrogen in 16.2 to 32.5 grams of amino acids.
Adequate calories should be administered simultaneously.

Patients receiving RenAmin® (Amino Acid) Injection should be monitored carefully and their electrolyte requirements individualized. Electrolyte supplementation may be required. This injection contains approximately 60 mEq acetate and 31 mEq chloride.

Electrolyte (phosphorous, potassium and magnesium) concentrations usually fall during administration of RenAmin® (Amino Acid) Injection. Particular care should be taken in the presence of cardiac arrhythmias or digitalis toxicity to assure that these electrolytes are supplemented when necessary.

Children:
Pediatric requirements vary depending upon growth, nutritional state and degree of renal insufficiency. A dosage of 0.5 to 1.0 gram of amino acids per kilogram body weight per day will meet the requirements of the majority of pediatric patients. Initial daily dosage should be low and increased slowly. More than one gram of essential amino acids per kilogram of body weight per day is not recommended. The total volume of nutritional solution, and the rate at which it is administered, will vary with the child’s age, nutritional and growth state, as well as the degree of renal failure. See Special Precautions in Pediatric Patients for additional information.
Maintenance vitamins, additional electrolytes and trace elements should be administered as required.

Central Vein Administration:
Hypertonic mixtures of amino acids and dextrose may be administered safely by continuous infusion through a central vein catheter with the tip located in the vena cava. In addition to meeting nitrogen needs, the administration rate is governed, especially during the

first few days of therapy, by the patient's tolerance to dextrose. Daily intake of amino acids and dextrose should be increased gradually to the maximum required dose as indicated by frequent determinations of urine and blood sugar levels.
Uremic patients frequently are glucose intolerant. Provision of adequate calories in the form of hypertonic dextrose may require the administration of exogenous insulin to prevent hyperglycemia and glycosuria.
Parenteral nutrition may be started at lower administration rates and with infusates containing lower concentrations of dextrose; dextrose content and rate may be gradually increased to estimated caloric needs as the patient's glucose tolerance increases. The patient's fluid, nitrogen and glucose tolerance should be the determining factor of the rate of administration.
Sudden cessation in administration of concentrated dextrose solutions may result in insulin reactions due to continued endogenous insulin production. Such solutions should be withdrawn slowly.

Peripheral Vein Administration:
For patients requiring parenteral nutrition in whom the central vein route is not indicated, this injection can be mixed with low concentration dextrose solutions and administered by peripheral vein with fat emulsions.
Intravenous fat emulsions provide approximately 1.1 kcal/mL (10%) or 2.0 kcal/mL (20%) and may be administered along with amino acid-dextrose solutions through a short Y-connector near the infusion site to supplement caloric intake. Fat, however, should not be the sole caloric intake since studies have indicated that glucose is more nitrogen sparing in the stressed patient.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Use of a final filter is recommended during administration of all parenteral solutions where possible.
Do not use unless solution is clear and vacuum is present. Unit must be used with a vented set or a nonvented set with a vented spike adapter.

RenAmin® (Amino Acid) Injection in the Pharmacy Bulk Package is intended for use in the preparation of sterile, intravenous admixtures. Additives may be incompatible with the fluid withdrawn from this container. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist, if available. When compounding admixtures, use aseptic technique. Mix thoroughly. Do not store any unused portion of RenAmin® (Amino Acid) Injection.
Solutions should be used promptly after mixing. Any storage should be under refrigeration and limited to a brief period of time, preferably less than 24 hours.

DIRECTIONS FOR USE OF THE PHARMACY BULK PACKAGE CONTAINER
For compounding only, not for direct infusion.
1. The Pharmacy Bulk Package is to be used only in a suitable work area such as a laminar flow hood (or an equivalent clean air compounding area).
2. Remove outer seal and metal disc.
3. Swab surface of stopper using approved technique.
4. Insert vented connector of solution transfer set and suspend unit. Refer to directions accompanying set.
Note: The closure shall be penetrated only one time with a suitable sterile transfer device or dispensing set which allows measured dispensing of the contents.
5. Once container closure has been penetrated, withdrawal of contents should be completed without delay. After initial entry, maintain contents at room temperature (25ºC/77ºF) and dispense within 4 hours.

HOW SUPPLIED
RenAmin® (Amino Acid) Injection is available in glass Pharmacy Bulk Packages as follows:

2A6222	250 mL	NDC 0338-0471-02
2A6223	500 mL	NDC 0338-0471-03

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended the product be stored at room temperature (25ºC/77ºF): brief exposure up to 40ºC does not adversely affect the product, Protect from light until immediately prior to use.
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